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EXAMINER	
GOLDBERG, JEANINE ANNE	

ART UNIT	PAPER NUMBER
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/241,636	HEATH ET AL.	
	Examiner	Art Unit	
	Jeanine A Goldberg	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *3/9/04; 5/24/04*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-10 and 12-62* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10 and 12-62* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This action is in response to the papers filed March 9, 2004 and May 24, 2004. Currently, claims 1-10, 12-62 are pending.

2. All arguments have been thoroughly reviewed but are deemed non-persuasive for the reasons which follow.

3. This action is made FINAL.

4. This action contains new grounds or rejection necessitated by amendment.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claims 1, 3-6, 15, 17-19, 22-24, 26, 28-30, 32-33, 37-38, 41, 44-49, 53, 54-58, 60 are rejected under 35 U.S.C. 102(e) as being anticipated by Harvey et al. (US Pat. 5.939,259, August 1999).

Harvey teaches a method and device for collecting and storing clinical samples for genetic analysis. Harvey teaches a process for characterizing DNA by isolating nucleic acids which comprises contacting a biological material with a solid support treated with a lysing reagent (i.e. a absorbent material that is impregnated with

chaotropic salt); b) treating the biological material with a DNA purifying agent (i.e. water and vortex), c) purifying the DNA from the remainder (i.e. supernatant) d) analyzing the purified DNA (i.e. PCR reactions and electrophoresis)(col. 5, lines 25-55)(limitations of Claim 1, 26, 54-55). Moreover, Harvey specifically teaches fabricating an absorbent material with a roll of 903 paper which is impregnated with guanidine thiocyanate solution having a concentration between 0.5M and 5.0 M (limitations of Claim 33, 37-38, 41, 56-58, 60). The paper is allowed to dry (col. 5, lines 10-22). Harvey teaches isolating DNA from fecal sources, saliva sources, and whole blood sources (limitations of Claim 5-6, 29-30, 31). Specifically, two separate squares of 903 paper are exposed to samples, one paper treated and the other paper untreated. The samples was allowed to dry and the papers was transferred to a centrifuge tube containing water and vortexed (col. 5, lines 30-35)(limitations of Claim 3, 28). The paper was further transferred to a second centrifuge tube containing water and placed on a heating block at 95 degrees for 30 minutes (col. 5, lines 35-40)(limitations of Claim 4, 44). The supernatant from each sample was amplified and analyzed by electrophoresis on a polyacylamide gel which were visualized by silver staining (Example 6)(limitations of Claim 15, 17-19, 22-24, 45-49, 52-53). Moreover Harvey specifically claims a method for collecting nucleic acids from a whole blood source by contacting a whole blood source with an adsorbent material that has a chaotropic salt impregnated, allowing the source to be absorbed on the absorbent material and eluting the nucleic acids into a solution that can be used in a nucleic acid amplification process (col. 8).

Thus, since Harvey has taught every limitation of the instant claims, Harvey anticipates the claimed invention.

Response to Arguments

The response traverses the rejection. The response asserts the reagents in the present invention are less hazardous than those contemplated by Harvey. The response asserts that substances such as guanidium and urea must be used at such high concentrations as 6M in solution to cause lysis (page 12 of response). This argument has been reviewed but is not convincing because it is unclear what the limitations of the newly added clause encompass. It is unclear what is encompassed by "low concentrations" as noted below in the 112/2nd necessitated by amendment. Further, Harvey teaches that chaotropic salts may be used and dried. The solutions can contain from about 0.1M to 6.0M salt concentrations, preferably 0.5M to 2.0M (col. 3, lines 25-35). Therefore, the arguments by the attorney that substances such as guanidium and urea must be used at such high concentrations as 6M in solution to cause lysis is merely argument and does not appear to be supported the objective evidence on the record. Harvey teaches that "other reagents can be added to the present invention in order to enhance lysis or disruption of intact cells absorbed onto the device (col. 5, lines 1-5). Therefore, Harvey teaches that the 0.5 to 2.0M chaotropic salt, such as guanidine (iso)thiocyanate is a lysing reagent that may be enhanced.

The response asserts that Harvey does not teaches that the immobilized concentration of chaotropes cause complete lysis of the cells (page 13 of response). This argument has been thoroughly reviewed, but is not found persuasive because the

claims do not require "complete lysis of the cells." Further, upon close examination of the claims, the claims do not require that the cells are lysed. The claims merely require that the sample is contacted with a solid support treated with a lysing reagent, purifying the DNA and analyzing. Thus, the claims are not limited to complete lysis of the cells as argued by the response.

Thus for the reasons above and those already of record, the rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1-3, 5-6, 12-21, 23-30, 32-33, 37, 39, 41, 45-51, 53-56, 58, 60-62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boom et al (5,234,809) in view of Shieh (US Pat. 6,054,039, April 2000).

Boom teaches methods of characterizing DNA. Boom discloses a process which involved contacting the biological material that contains DNA with a solid support that had been treated with a lysing reagent (i.e. a chaotropic substance), treating the biological material with a purifying reagent, and purifying the DNA (col. 4, lines 3-59). The chaotropic substance (lysing reagent) is contacted with silica particles (solid support). The biological material is then treated with purifying reagents, and the

remainder of the biological matter is purified (washing buffer, alcohol washing solution and acetone. Additionally, the process described by Boom produces DNA which can be further used to "demonstrate NA sequences by means of an amplification method such as the PCR method...." (col.4, lines 48-50)(limitations of claims 24-27 and 45-46). Since Boom teaches that the Gus SCN (i.e. the lysis reagent) is added to the solid support (i.e. the silica beads) prior to addition of biological material, Boom is inherently teaching a solid support to which a lysing reagent is "bound." The term "bound" is being broadly interpreted to mean loosely and transiently in contact with the solid support. As described in Boom, the DNA may be eluted from the solid support by means of an eluting reagent (col.4, line 33). Boom teaches an eluting reagent can be TE buffer, aqua bidest or PCR buffer. Boom further teaches the process where in the solid support is contained in a single vessel (col.4, lines 34-36) (limitations of claims 3 and 28). Boom demonstrates the use of isolating nucleic acids from a nucleic acid-containing biological material (col. 1, lines 10-20). The biological material stated includes tissues, cell cultures, blood, urine, and saliva (body fluids)(limitations of claims 5-6, 29-30). The nucleic acid was taught to be examined by gel electrophoresis (col. 10, lines 13-24) (limitations of claims 12-17, 19, 21, 47-49). This method may be used for characterizing the biological material and monitoring impurities. Yields were also taught in example A1 (col. 12, lines 46-48)(limitations of claim 18). Eluted DNA was treated with a restriction enzyme, electrophoresed and visualized (col. 12 65-68) (limitations of claims 21 and 50). Boom also teaches hybridization analysis of the isolated nucleic acids (col. 9, lines 19-21)(limitations of claims 23 and 53). Boom teaches a method which can "provide a

process with which nucleic acid can be isolated immediately..." (col. 1, lines 64-67) (limitation of claim 32). Boom teaches lysis buffers containing Tris (buffer), aqua bidest, GuSCN, and EDTA (col. 6, lines 39-68).

Boom does not explicitly teach using a solid support in which the lysing reagent is bound, and unbound lysing reagent is removed prior to the contacting of the biological treatment.

However, Shieh teaches a method for lysing cells. Specifically, Shieh teaches the modification of a membrane strip to produce lysis of red blood cells that contacts it (col. 6, lines 17-20). Shieh teaches that membranes such as polymer treated glass fibers, polyamides, cellulose, polyesters may be used (col. 10, lines 42-57)(limitations of Claims 33). Shieh teaches preparing a lysing component by treating the membranes with a lysing agent (col. 10, lines 65-67). Shieh teaches that lysing agents included Mega 8, Triton X, lauryl sulfate salts, TEA sals, sodium salt, among numerous others (col. 11, lines 1-10)(limitations of Claims 61-62). Furthermore, Shieh teaches that the lysing agent may be coated onto the membrane by any method used in the art for coating solutions onto films such as dip coating an aqueous solution or disperson of the lysing solution onto the membrane and allowing to dry (col. 11, lines 10-20). As provided in Example 1D, a cell lysing membrane was prepared (col. 12, lines 8-18). Furthermore, Shieh teaches that "this component caused lysis of whole blood when it passed across the membrane (col. 14, lines 31-33). Shieh teaches that the method and sensor may be used "on the spot: at home, in a physicians office or in a hospital room". Shieh also teaches the sensor is low cost and disposable (col. 15, lines 55-60).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Boom, which characterizes DNA using a solid support, lysing reagent and a biological material with a pre-treated membrane of Shieh. Shieh teaches that biological samples may be lysed using a pre-treated membrane such that lysis is caused when a sample is passed across the membrane. The ordinary artisan would have been motivated to have produced a solid support which was pre-treated with a lysing reagent, as taught by Shieh, for the expected benefit taught by Shieh as low cost and disposability. The ordinary artisan would also have been motivated to have prepared the pre-treated lysing membranes, of Shieh, for use in the method, of Boom, for the expected benefit of convenience. Moreover, the skilled artisan would have had a reasonable expectation of success for analyzing DNA from a solid support that was pretreated with a lysing reagent since Boom teaches a method in which all three components, a lysing reagent, solid support and nucleic acid sample, were contacted with successful results. Thus, the skilled artisan would have combined the teachings of Boom with the teachings of Shieh.

Response to Arguments

The response traverses the rejection. The response asserts that Boom requires the use of highly toxic chaotropic substances which are not the lysing reagents of the instant invention. This argument has been thoroughly review, but not convincing because, Claims 1-3, 5-6, 12-21, 23-30, 32-33, 37, 39, 41, 45-51, 53-56, 58, 60-62 are not drawn to any specific lysing reagent, the claims are have been amended to a lysing

reagent which comprises "essentially low concentrations of reagents." As discussed below, this is a relative term which has not been defined by the claims or specification. Thus, the lysing reagent of Boom has been interpreted to be within the scope of the claims.

Further the response argues that Boom teaches the combination of an excess of chaotropic lysing reagent to enable complete lysis of the biological sample. This argument has been thoroughly reviewed, but is not found persuasive because the claims are not drawn to any particular lysing reagent and more particularly are not drawn to any efficiency or completeness of lysis as argued by the response. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., complete lysis of the biological sample) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

The response asserts that the skilled artisan would not be motivated to immobilize the chaotropic reagents as taught by Boom on the membrane of Shieh. The response asserts because Boom requires a chaotrope in excess to cause lysis teaches away from applying a very small fractional amount of that lysing reagent to a membrane to cause lysis. This argument has been thoroughly reviewed, but is not found persuasive because while immobilizing a small fractional amount of the lysing reagent of Boom onto a solid support may not have caused complete lysis the ordinary artisan

would have recognized that solid supports with lysing reagents dried thereupon would have had the expected benefit of convenience, low cost and disposability, as taught by Shieh. Moreover, the ordinary artisan would have recognized that in order to lyse cells, and nuclear membranes, different lysing reagents would be necessary. It would have been obvious to use the lysing reagents of Boom to lyse cells to analyze nucleic acids because the lysing reagents of Boom are suitable for lysing cells for nucleic acid isolation. The teachings of Shieh illustrate that a lysing matrix may be formed by drying the lysing solution onto the membrane prior to contact with a biological material. The combination of this teaching that drying the lysing solution onto the membrane prior to contact with a biological material and the teachings of Boom that DNA may be characterized by lysing a biological material, using a purifying reagent, purifying, and analyzing the DNA. The art clearly illustrates a lysing reagent bound to a solid support and removing any unbound lysing reagent prior to the contact with a biological material. Thus, as provided above, "The ordinary artisan would have been motivated to have produced a solid support which was pre-treated with a lysing reagent, as taught by Shieh, for the expected benefit taught by Shieh as low cost and disposability. The ordinary artisan would also have been motivated to have prepared the pre-treated lysing membranes, of Shieh, for use in the method, of Boom, for the expected benefit of convenience. While complete lysis of cells may not occur, the claim does not require a limitation of any particular amount of lysis or particular lysing reagent.

Thus for the reasons above and those already of record, the rejection is maintained.

7. Claims 1-20, 24-33, 37-41, 44-49, 54-62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Deggerdal (WO 96/18731) in view of Shieh (US Pat. 6,054,039, April 2000).

Deggerdal teaches methods of characterizing DNA. Deggerdal discloses a "method of isolating nucleic acid from a sample, said method comprising contacting said sample with a detergent and a solid support, whereby soluble nucleic acid in said sample is bound to the support, and separating said support with bound nucleic acid from the sample" (pg 5, para 2). Deggerdal teaches that the "nucleic acid-containing sample may be contacted with the detergent and solid phase which may be added to the sample prior to, simultaneously with, or subsequently to the detergent (which functions in the method to lyse)"(pg 7, para 3, lines 22-29). Deggerdal is inherently teaching a solid support to which a lysing reagent is "bound." The term "bound" is being broadly interpreted to mean loosely and transiently in contact with the solid support. The solid support was contained in a vessel (pg 26, line 18). Deggerdal teaches isolation of nucleic acids and the elution of the nucleic acid by heating to 65 C for 5-10 minutes (pg 12, para 3, line 3)(limitations of claims 4 and 44). The samples may be of "any material containing nucleic acid" (pg 6, para 1, line 1-3)(limitations of claims 5-7 and 29-31). Deggerdal teaches a method of DNA isolation from cultured cells which indicates the number of cells used as starting material (pg 33, line 1) (limitations of claims 8-10). The purified DNA was then analyzed by PCR and visualized on agarose gel electrophoresis (pg 20, lines 29-32). Detection of extra bands indicated contamination (pg 17, lines 26-27). The solid support was taught to be made of "glass, silica, latex or a polymeric

material" (pg 9, para 3)(limitations of claim 33). Deggerdal teaches an example where cells were lysed using DNA DIRECT Dynabeads and the lysate from each sample was further characterized (pg 35, lines 6-35)(limitations of claim 11). Deggerdal teaches the lysing reagent as a detergent. This detergent may be supplied in simple aqueous solution (pg 8, line 7). Further any suitable buffer (Tris) is taught. The reagent may also include components such as enzymes, chelating agents and reducing agents (pg 8, lines 7-23) (limitations of claims 37-41).

Deggerdal does not explicitly teach using a solid support in which the lysing reagent is bound, and unbound lysing reagent is removed prior to the contacting of the biological treatment.

However, Shieh teaches a method for lysing cells. Specifically, Shieh teaches the modification of a membrane strip to produce lysis of red blood cells that contacts it (col. 6, lines 17-20). Shieh teaches that membranes such as polymer treated glass fibers, polyamides, cellulose, polyesters may be used (col. 10, lines 42-57)(limitations of Claims 33). Shieh teaches preparing a lysing component by treating the membranes with a lysing agent (col. 10, lines 65-67). Shieh teaches that lysing agents included Mega 8, Triton X, lauryl sulfate sals, TEA sals, sodium salt, among numerous others (col. 11, lines 1-10)(limitations of Claims 61-62). Furthermore, Shieh teaches that the lysing agent may be coated onto the membrane by any method used in the art for coating solutions onto films such as dip coating an aqueous solution or disperson of the lysing solution onto the membrane and allowing to dry (col. 11, lines 10-20). As provided in Example 1D, a cell lysing membrane was prepared (col. 12, lines 8-18).

Furthermore, Shieh teaches that "this component caused lysis of whole blood when it passed across the membrane (col. 14, lines 31-33). Shieh teaches that the method and sensor may be used "on the spot: at home, in a physicians office or in a hospital room". Shieh also teaches the sensor is low cost and disposable (col. 15, lines 55-60).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Deggerdal, which characterizes DNA using a solid support, lysing reagent and a biological material with the method and pre-treated membrane of Shieh. Shieh teaches that biological samples may be lysed using a pre-treated membrane such that lysis is caused when a sample is passed across the membrane. The ordinary artisan would have been motivated to have produced a solid support which was pre-treated with a lysing reagent, as taught by Shieh, for the expected benefit taught by Shieh as low cost and disposability. The ordinary artisan would also have been motivated to have prepared the pre-treated lysing membranes, of Shieh, for use in the method, of Deggerdal, for the expected benefit of convenience. Moreover, the skilled artisan would have had a reasonable expectation of success for analyzing DNA from a solid support that was pretreated with a lysing reagent since Deggerdal teaches a method in which all three components, a lysing reagent, solid support and nucleic acid sample, were contacted with successful results. Thus, the skilled artisan would have combined the teachings of Deggerdal with the teachings of Shieh.

Response to Arguments

The response traverses the rejection. The response asserts the aforementioned discussion detailing the differences between the instant invention and the cited art of Boom and Shieh overcome the rejection cited by the Examiner. This argument has been reviewed but is not convincing .

The response asserts that the skilled artisan would not be motivated to immobilize the chaotropic reagents as taught by Deggerdal on the membrane of Shieh. The response asserts because Deggerdal requires an excess to cause lysis. This argument has been thoroughly reviewed, but is not found persuasive because while immobilizing a small fractional amount of the lysing reagent of Deggerdal onto a solid support may not have caused complete lysis the ordinary artisan would have recognized that solid supports with lysing reagents dried thereupon would have had the expected benefit of convenience, low cost and disposability, as taught by Shieh. Moreover, the ordinary artisan would have recognized that in order to lyse cells, and nuclear membranes, different lysing reagents would be necessary. It would have been obvious to use the lysing reagents of Deggerdal to lyse cells to analyze nucleic acids because the lysing reagents of Deggerdal are suitable for lysing cells for nucleic acid isolation. The teachings of Shieh illustrate that a lysing matrix may be formed by drying the lysing solution onto the membrane prior to contact with a biological material. The combination of this teaching that drying the lysing solution onto the membrane prior to contact with a biological material and the teachings of Deggerdal that DNA may be characterized by lysing a biological material, using a purifying reagent, purifying, and analyzing the DNA. The art clearly illustrates a lysing reagent bound to a solid support

and removing any unbound lysing reagent prior to the contact with a biological material. Thus, as provided above, "The ordinary artisan would have been motivated to have produced a solid support which was pre-treated with a lysing reagent, as taught by Shieh, for the expected benefit taught by Shieh as low cost and disposability. The ordinary artisan would also have been motivated to have prepared the pre-treated lysing membranes, of Shieh, for use in the method, of Deggerdal, for the expected benefit of convenience. While complete lysis of cells may not occur, the claim does not require a limitation of any particular amount of lysis or particular lysing reagent.

Thus for the reasons above and those already of record, the rejection is maintained.

8. Claims 38 and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boom (5,234,809) in view of Shieh (US Pat. 6,054,039, April 2000) as applied to Claims 1-3, 5-6, 11-21, 23-30, 32-33, 37, 39, 41, 45-51, 53-56, 58, 60-62 above, and further in view of in view of Deggerdal (WO 96/18731).

Neither Boom, nor Shieh teaches a lysing reagent which does not contain a buffer.

Deggerdal, however, teaches a lysing reagent as a detergent. This detergent may be supplied in simple aqueous solution (pg 8, line 7). Further any suitable buffer (Tris) is taught. The reagent may also include components such as enzymes, chelating agents and reducing agents (pg 8, lines 7-23) (limitations of claims 37-41).

Therefore, it would have been prima facie obvious to one of ordinary skill at the time of the invention was made to have modified the method of Boom in view of Shieh to include the use of the lysing reagents taught in Deggerdal. The ordinary artisan would have been motivated to use the lysing reagents taught in Deggerdal because the lysing reagents taught in Deggerdal were readily available.

Response to Arguments

The response traverses the rejection. The response asserts the aforementioned discussion detailing the differences between the instant invention and the cited art overcome the rejection cited by the Examiner. This argument has been reviewed but is not convincing because the Shieh teaches a solid support with lysing material dried upon the support to serve as a lysing matrix. Thus for the reasons above and those already of record, the rejection is maintained.

9. Claims 23 and 52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Deggerdal (WO 96/18731) in view of Shieh (US Pat. 6,054,039, April 2000) as applied to Claims 1-20, 24-33, 37-41, 44-49, 54-62 above and further in view of Boom (5,234,809).

Neither Deggerdal, nor Shieh specifically teaches conducting a hybridization analysis on the amplified DNA.

However, Boom teaches hybridization analysis of the isolated nucleic acids (col. 9, lines 19-21).

Therefore, it would have been prima facie obvious to one of ordinary skill at the time of the invention was made to have applied the method of Deggerdal in view of Shieh to include the method of hybridization reactions as used in the method of Boom. The ordinary artisan would have been motivated to have conducted hybridization reactions taught in the method of Boom on the isolated DNA obtained from the Deggerdal method to further characterize the DNA sample.

Response to Arguments

The response traverses the rejection. The response asserts the aforementioned discussion detailing the differences between the instant invention and the cited art overcome the rejection cited by the Examiner. This argument has been reviewed but is not convincing because the Shieh teaches a solid support with lysing material dried upon the support to serve as a lysing matrix. Thus for the reasons above and those already of record, the rejection is maintained.

10. Claims 7, 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boom (5,234,809) in view of Shieh (US Pat. 6,054,039, April 2000) as applied to Claims 1-3, 5-6, 11-21, 23-30, 32-33, 37, 39, 41, 45-51, 53-56, 58, 60-62 above or Harvey et al. (US Pat. 5.939,259, August 1999) and further in view of Su (5,804,684).

Harvey teaches a method and device for collecting and storing clinical samples for genetic analysis. Harvey teaches a process for characterizing DNA by isolating nucleic acids which comprises contacting a biological material with a solid support treated with a lysing reagent (i.e. a absorbent material that is impregnated with

chaotropic salt); b) treating the biological material with a DNA purifying agent (i.e. water and vortex), c) purifying the DNA from the remainder (i.e. supernatant) d) analyzing the purified DNA (i.e. PCR reactions and electrophoresis)(col. 5, lines 25-55)(limitations of Claim 1, 26, 54-55). Moreover, Harvey specifically teaches fabricating an absorbent material with a roll of 903 paper which is impregnated with guanidine thiocyanate solution having a concentration between 0.5M and 5.0 M (limitations of Claim 33, 37-38, 41, 56-58, 60). The paper is allowed to dry (col. 5, lines 10-22). Harvey teaches isolating DNA from fecal sources, saliva sources, and whole blood sources (limitations of Claim 5-6, 29-30, 31). Specifically, two separate squares of 903 paper are exposed to samples, one paper treated and the other paper untreated. The samples was allowed to dry and the papers was transferred to a centrifuge tube containing water and vortexed (col. 5, lines 30-35)(limitations of Claim 3, 28). The paper was further transferred to a second centrifuge tube containing water and placed on a heating block at 95 degrees for 30 minutes (col. 5, lines 35-40)(limitations of Claim 4, 44). The supernatant from each sample was amplified and analyzed by electrophoresis on a polyacylamide gel which were visualized by silver staining (Example 6)(limitations of Claim 15, 17-19, 22-24, 45-49, 52-53). Moreover Harvey specifically claims a method for collecting nucleic acids from a whole blood source by contacting a whole blood source with an adsorbent material that has a chaotropic salt impregnated, allowing the source to be absorbed on the absorbent material and eluting the nucleic acids into a solution that can be used in a nucleic acid amplification process (col. 8).

Neither Boom, nor Shieh, nor Harvey specifically teaches biological material from the group consisting of environmental samples taken from air, water, sediment and soil.

However, Su teaches a list of samples which includes "any type of biological sample....environmental, nutritional, scientific or industrial significance" (col.8, lines 3-16).

Therefore, it would have been prima facie obvious to one of ordinary skill at the time of the invention was made to have applied the method of Boom in view of Shieh or Harvey to include the use of environmental samples as the biological starting material as used in the method of Su. The ordinary artisan would have been motivated to have sampled the biological materials from the environment because environmental samples are a well known source of clinically important DNA containing organisms whose detection is necessary to prevent disease spread, for example.

Response to Arguments

The response traverses the rejection. The response asserts the aforementioned discussion detailing the differences between the instant invention and the cited art overcome the rejection cited by the Examiner. This argument has been reviewed but is not convincing because the Shieh teaches a solid support with lysing material dried upon the support to serve as a lysing matrix. Thus for the reasons above and those already of record, the rejection is maintained.

11. Claims 42-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boom (5, 804,684) in view of Shieh (US Pat. 6,054,039, April 2000) as applied to

Claims 1-3, 5-6, 11-21, 23-30, 32-33, 37, 39, 41, 45-51, 53-56, 58, 60-62 above or Deggerdal (WO 96/18731) in view of Shieh (US Pat. 6,054,039, April 2000) as applied to Claims 1-20, 24-33, 37-41, 44-49, 54-62 above or Harvey et al. (US Pat. 5.939,259, August 1999) as applied to Claims 7, 31 above and further in view of Su (5,804684).

Neither Boom in view of Shieh nor Deggerdal in view of Shieh nor Harvey specifically teach the eluting reagent as specified in the claims.

However, Su teaches the elution buffer to be 5 mM Tris HCl, pH 9, and 0.5 mM EDTA (col. 10, line 17).

Therefore, it would have been prima facie obvious to one of ordinary skill at the time of the invention was made to have modified the method of Boom in view of Shieh or Deggerdal in view of Shieh or Harvey to include the use of the elution buffer described in the method of Su. The ordinary artisan would also have expected that using the elution buffer of Su in the method of Boom or Deggerdal or Harvey with the elution buffer described in Su would have provided equivalent results.

Response to Arguments

The response traverses the rejection. The response asserts the aforementioned discussion detailing the differences between the instant invention and the cited art overcome the rejection cited by the Examiner. This argument has been reviewed but is not convincing because the Shieh teaches a solid support with lysing material dried upon the support to serve as a lysing matrix. Thus for the reasons above and those already of record, the rejection is maintained.

12. Claims 22 and 51-52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boom (5, 804,684) in view of Shieh (US Pat. 6,054,039, April 2000) as applied to Claims 1-3, 5-6, 11-21, 23-30, 32-33, 37, 39, 41, 45-51, 53-56, 58, 60-62 above or Deggerdal (WO 96/18731) in view of Shieh (US Pat. 6,054,039, April 2000) as applied to Claims 1-20, 24-33, 37-41, 44-49, 54-62 above or Harvey et al. (US Pat. 5.939,259, August 1999) as applied to Claims 7, 31 above and further in view of Sambrook (Molecular Cloning).

Neither Boom in view of Shieh nor Deggerdal in view of Shieh nor Harvey specifically teach sequencing the purified DNA.

However, Sambrook teaches the analysis of DNA by nucleic acid sequencing (13.3). Sambrook teaches that the sequences provide the advantage of determining the sequence of nucleotides in a particular DNA molecule.

Therefore, it would have been prima facie obvious to one of ordinary shill at the time of the invention was made to have modified the method of Boom or Deggerdal in view of Shieh or Harvey to include the sequencing analysis method taught by Sambrook in order to make the claimed invention as a while. The ordinary artisan would be motivated to have sequenced the purified DNA obtained by the Boom method in order to have achieved the expected advantage of determining the sequence of nucleotides of the isolated DNA.

Response to Arguments

The response traverses the rejection. The response asserts the aforementioned discussion detailing the differences between the instant invention and the cited art

overcome the rejection cited by the Examiner. This argument has been reviewed but is not convincing because the Shieh teaches a solid support with lysing material dried upon the support to serve as a lysing matrix. Thus for the reasons above and those already of record, the rejection is maintained.

13. Claims 33 and 35-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boom (5, 804,684) in view of Shieh (US Pat. 6,054,039, April 2000) as applied to Claims 1-3, 5-6, 11-21, 23-30, 32-33, 37, 39, 41, 45-51, 53-56, 58, 60-62 above or Deggerdal (WO 96/18731) in view of Shieh (US Pat. 6,054,039, April 2000) as applied to Claims 1-20, 24-33, 37-41, 44-49, 54-62 above and further in view of Arnold (5,599,667).

14. Claims 35-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harvey et al. (US Pat. 5.939,259, August 1999) as applied to Claims 7, 31 above in view of Arnold (5,599,667).

Neither Boom, Deggerdal, nor Shieh, nor Harvey specifically teach using polyolefin as a solid support wherein polyolefin is hydrophilic and has a charge.

However, Arnold teaches polycationic solid supports that can be used purification of nucleic acids (see abstract). The polycationic support matrix is taught to include inorganic and organic materials which include glasses, polyolefins and polysaccharides (col.8, lines 55-62).

Therefore, it would have been prima facie obvious to one of ordinary skill at the time of the invention was made to have modified the method of Boom or Deggerdal in

view of Shieh or Harvey to include the solid supports of Arnold in order to make the claimed invention as a whole. The ordinary artisan would be motivated to have substituted polyolefins as a solid support in the Boom or Deggerdal or Harvey method because Arnold taught that polyolefins and glass are both suitable for DNA isolation because they meet the same "principle requirement" of "not unduly adsorbing either contaminants or nucleotide probes (col. 8, lines 61-64). Consequently Arnold shows that the silica of Boom or Deggerdal and the polyolefins of the claims are equivalent.

Response to Arguments

The response traverses the rejection. The response asserts the aforementioned discussion detailing the differences between the instant invention and the cited art overcome the rejection cited by the Examiner. This argument has been reviewed but is not convincing because the Shieh teaches a solid support with lysing material dried upon the support to serve as a lysing matrix. Thus for the reasons above and those already of record, the rejection is maintained.

15. Claim 34 is rejected under 35 U.S.C. 103(a) as being unpatentable over Boom (5, 804,684) in view of Shieh (US Pat. 6,054,039, April 2000) or Deggerdal (WO 96/18731) in view of Shieh (US Pat. 6,054,039, April 2000) or Harvey et al. (US Pat. 5.939,259, August 1999) and further in view of Arnold (5,599,6667) as applied to claim 33, 35-36 above, and further in view of Hasebe (5,151,345).

Arnold teaches polycationic solid supports that can be used purification of nucleic acids (see abstract). The polycationic support matrix is taught to include inorganic and

organic materials which include glasses, polyolefins and polysaccharides (col.8, lines 55-62).

However, neither Boom or Deggerdal nor Arnold specifically teaches that polyolefin is a mixture of low density polyethylene and polypropylene fibers.

However, Hasebe teaches that "a polyolefin resin is preferred, and low-density polyethylene, high-density polyethylene...or a blend thereof is preferably used"(col. 11, lines 32-39).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time of the invention was made to combine the methods of Boom or Deggerdal or Harvey and Arnold as discussed above and use the types of polyolefins taught by Hasebe. As Arnold teaches that "polyolefins" may be used in DNA isolation, one of ordinary skill in the art would have been motivated to use a preferred polyolefin resin.

Response to Arguments

The response traverses the rejection. The response asserts the aforementioned discussion detailing the differences between the instant invention and the cited art overcome the rejection cited by the Examiner. This argument has been reviewed but is not convincing because the Shieh teaches a solid support with lysing material dried upon the support to serve as a lysing matrix. Thus for the reasons above and those already of record, the rejection is maintained.

New Grounds of Rejection Necessitated by Amendment
Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-10, 12-53 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 1-10, 12-53 are indefinite over the recitation "the lying reagent." The claim does not particularly set forth a "lying reagent." The claims are presumed to be referring to the "lysing" reagent. This may be a typographical error. Appropriate correction is required. Further, the term "essentially comprises low concentrations of reagents" in claims 1, 2, 26-27 is a relative term which renders the claim indefinite. The term "essentially comprises low concentrations of reagents" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is unclear what is encompassed by low concentrations of reagents. The specification nor the claims sets for the limitations or the ranges encompassed by "essentially comprises low concentrations of reagents." Thus, the metes and bounds of the claimed invention are unclear.

Conclusion

16. **No Claims are allowable over the prior art.**

17. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

18. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

A) Harvey et al. Clinical Chem. Vol. 41, pages S108, No. 6, 1995. Harvey teaches impregnating paper with chaotropic salts and their efficiencies. DNA from blood spots collected on guanidine impregnated paper was released in high levels and contained little if any inhibitory substance for PCR. Blood collection paper treated with this chaotrope provides a rapid and reproducible method for the preparation of DNA from died blood spots.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is (571) 272-0743. The examiner can normally be reached Monday-Friday from 7:00 a.m. to 4:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (571) 272-0782.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

J. Goldberg

Jeanine Goldberg
Patent Examiner
August 2, 2004